Brief Communication

Perspectives on the Treatment of Orthostatic Hypotension Associated With Hypertension

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Orthostatic hypotension is defined as a reduction in systolic blood pressure of at least 20 mmHg or a reduction in diastolic blood pressure of at least 10 mmHg within 3 minutes of standing up. The frequent and rapid cardiovascular adjustments essential for homeostatic control of blood pressure are not accomplished in patients with orthostatic hypotension, who experience symptomatic and often extreme high and low blood pressure variations. In most cases, the underlying cause of orthostatic hypotension is not amenable to correction, and patients have lifelong symptoms. Current treatment strategies are directed at improving patients' symptoms by raising blood pressure. Such interventions, however, do not address the coincident problems of extreme high blood pressure, nocturnal hypertension, and resultant end-organ damage present in these patients. [*Hong Kong J Nephrol* 2005;7(1):51–3]

Key words: hypertension, orthostatic hypotension

直立性低血壓的定義，是病人在站立後3分鐘內收縮壓降幅達至少 20 mmHg、或舒張壓降幅達至少 10 mmHg。受影響的人未能因應體位的變化，從而作出迅速及適當的心血管調適，導致血壓未能維持在足夠的水平，病人亦可能會出現低血壓的症狀。對於大部分的患者而言，直立性低血壓缺乏有效的矯治方法，病人可能會終身受症狀影響。目前的治療方式是透過血壓的上調，以改善患者的症狀。然而，對於同時發生極端高血壓或夜間高血壓的病人，這類療法缺乏助益，亦未能有效預防隨之而來的終器傷朗。

Orthostatic hypotension is defined as a reduction in systolic blood pressure of at least 20 mmHg or a reduction in diastolic blood pressure of at least 10 mmHg within 3 minutes of standing up [1]. It may be associated with neurologic and non-neurologic entities, and 24-hour ambulatory blood pressure monitoring may demonstrate a reversal of circadian patterns with nocturnal hypertension [2]. The frequent and rapid cardiovascular adjustments essential for homeostatic control of blood pressure are not accomplished in patients with orthostatic hypotension, who experience symptomatic and often extreme high and low blood pressure variations (Figure 1). In most cases, the underlying cause of orthostatic hypotension is not amenable to correction, and patients have lifelong symptoms [3]. Current treatment strategies are directed at improving patients' symptoms by raising blood pressure [4]. Such interventions, however, do not address the coincident problems of extreme high blood pressure, nocturnal hypertension, and resultant end-organ damage present in these patients [5,6].

Symptoms and target-organ damage are caused by fluctuations in blood pressure control, and a cure for orthostatic hypotension is currently unavailable for most patients, thus necessitating strategies that use combinations of nonpharmacologic and pharmacologic interventions to attenuate episodes of hypotension and hypertension. We propose that, initially, attempts be made to raise the low end of blood pressure to a level that provides some symptomatic relief to the patient (Figure 2). In our clinical experience, a standing systolic blood pressure of 90–120 mmHg provides symptomatic relief to most patients. This level can be achieved by the gradual introduction of various general and

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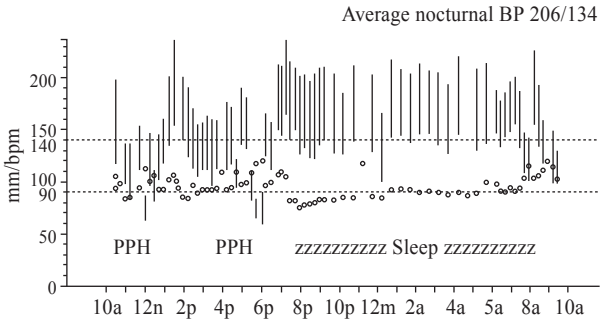

Figure 1. Twenty-four-hour ambulatory blood pressure (24-hour ABP) monitoring demonstrates characteristic blood pressure (BP) fluctuations in a patient with orthostatic hypotension. The ABP monitor concurrently recorded heart rate (circles) and BP (vertical lines) every 15 minutes during waking hours, and every 30 minutes while asleep (z). The maximum of each vertical line represents systolic BP, whereas the minimum represents diastolic BP; horizontal dashed lines represent the upper limits of the reference ranges for systolic and diastolic BPs. PPH = postprandial hypotension.

Table. Treatment of orthostatic hypotension

General measures
Exclude treatable medical disorders, medications, and volume depletion
Avoid prolonged standing, and sudden posture changes [6]
Avoid alcohol, hot environments, and rigorous exercise
Frequent small meals; two cups of coffee in the morning [7,8]
Sleep with the bed-head elevated (15–20°) [9]
Nonpharmacologic measures to elevate blood pressure
Frequent ingestion of 250–300 mL of water [8]
Salt added to diet (10 g/d) [10]
Compression stockings [11]
Abdominal binder [11]
Pharmacologic measures to increase blood pressure
Midodrine hydrochloride
Fludrocortisone acetate
Sympathomimetics
Erythropoietin (if anemia is present)
Others
Pharmacologic measures to decrease blood pressure
Angiotensin-converting enzyme inhibitors
α_2-adrenergic receptor agonists
α_1-adrenergic receptor antagonists
β-adrenergic receptor antagonists with intrinsic sympathomimetic activity

nonpharmacologic measures (Table), which aim to increase blood pressure by augmenting blood volume, and to promote venous return by translocating blood from the leg veins and splanchnic vascular bed. Collectively, these measures can have pronounced circulatory effects. Drinking water can elicit a potent pressor response for a short duration (60–90 minutes) [8], and frequent water ingestion can attenuate symptoms. For patients who fail to attain the target standing systolic blood pressure of 90–120 mmHg by the above interventions, pharmacologic agents can be used. Midodrine hydrochloride exerts its vasopressor effects via activation of α-adrenergic receptors in the arteriolar and venous vasculature, and such effects last for 3–4 hours [12]. Fludrocortisone acetate possesses potent mineralocorticoid properties and has a plasma half-life of 3.5 hours and a biological half-life of 36 hours [13]. Sympathomimetics, erythropoietin, intranasal desmopressin, indomethacin, nadolol, pindolol, and other agents have been advocated for the amelioration of orthostatic hypotension, although their clinical efficacy is uncertain. Clinicians should exercise caution to avert the adverse consequences of an exaggerated hypertensive response, such as renal impairment or cardiac failure [14].

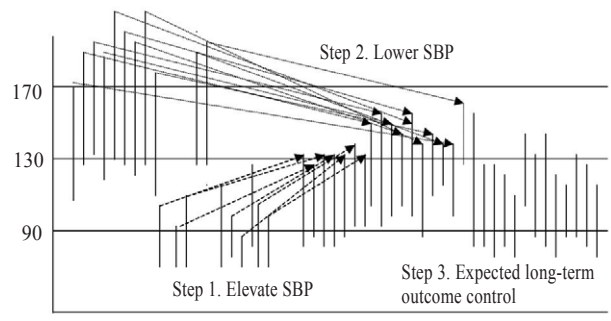

Figure 2. Hypothetical outcomes after proposed treatment for orthostatic hypotension. SBP = systolic blood pressure.

The abovementioned interventions may be effective in raising the lower end of the blood pressure spectrum, but may also lead to worsening of the higher end of the blood pressure spectrum (Figure 2). The resulting elevated blood pressure is managed with antihypertensive medications as needed to achieve a supine systolic blood pressure of less than 140 mmHg. Clonidine, an α_2-adrenergic receptor agonist, has been used successfully to control blood pressure lability [4], but angiotensin-converting enzyme inhibitors may have the advantage of also inhibiting the progression of target-organ damage, including nephropathy and cardiac disease [15]. Diuretics are best avoided, but β-adrenergic receptor blockers with intrinsic sympathomimetic activity and α_1-adrenergic receptor antagonists may be helpful.

An integral part of this approach to blood pressure control is active patient and family participation and easy access to the treating physician, such that the strategy provides assurance, hope, and empowerment

to the patient. Patients should measure their blood pressure daily in the morning and at bedtime, in both the upright and supine positions, and they should chart their progress, make necessary changes to their nonpharmacologic prescriptions under predefined criteria, and regularly follow up with the treating physician.

Various questions remain regarding the management of orthostatic hypotension, and ongoing basic and clinical research will hopefully clarify these issues. Current treatment strategies, regardless of the specific medication used, need to be directed at both symptom relief and prevention of end-organ damage. The incorporation of strategies for preventing cardiovascular mortality also seems prudent.

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